Contemporary open aortic arch repair with selective cerebral perfusion in the era of endovascular aortic repair

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Objective: With the recent advance of endovascular aortic repair, conventional open repair for aortic arch lesions should be reassessed. We reviewed our contemporary open arch repair with selective antegrade cerebral perfusion by way of the axillary artery with deep or moderate hypothermia.

Methods: From 2001 to 2011, 1007 patients (median age, 72 years) underwent open arch repair with selective cerebral perfusion through the right axillary artery and hypothermic circulatory arrest: deep (<25°C) in 48% and moderate (25°-28°C) in 52%. Of the 1007 patients, 73% underwent total arch replacement and 26% emergent surgery for aneurysm rupture or acute aortic dissection.

Results: The early mortality was 4.7% for all patients. Permanent and temporary neurologic dysfunction occurred in 3.5% and 6.7%, respectively. No spinal cord injury occurred, even with moderate hypothermia. The independent predictors of in-hospital mortality included chronic obstructive pulmonary disease, liver dysfunction, chronic kidney disease, and concomitant coronary artery bypass. The independent predictors of permanent neurologic dysfunction included cerebrovascular disease, emergency surgery, and concomitant coronary artery bypass. The cumulative survival rate was 80.4% and 71.2% at 5 and 8 years, respectively. Freedom from reoperation related to the initial arch repair was 98.0% and 96.9% at 5 and 8 years, respectively.

Conclusions: Conventional open arch repair yielded satisfactory outcomes and should remain the standard therapy, with good long-term durability in all but high-risk patients. (J Thorac Cardiovasc Surg 2013;145:S72-7)

Open surgical repair for aortic arch aneurysm is associated with considerable mortality and morbidity, especially stroke. However, its outcome has been dramatically improved by innovations in surgical technique, including brain protection, in the past 2 decades. In particular, the widespread use of antegrade selective cerebral perfusion (SCP) for cerebral protection has contributed to the reduction in mortality and stroke rate.[1-4] However, thoracic endovascular aortic repair (TEVAR) has been recognized as an alternative therapeutic option for thoracic aortic aneurysm, and it has been attempted, mainly for high-risk patients. Although this new technology was initially applied for descending aortic aneurysm, its adoption has extended to complex aortic arch lesions, predominantly in conjunction with several debranching techniques of the arch vessels as a less-invasive alternative: hybrid TEVAR.[5,6] Thus, contemporary open arch repair needs to be reassessed as a benchmark for consideration of the optimal therapeutic strategy for aortic arch aneurysm. In the present study, the results with our well-established contemporary open arch repair procedure during the past decade—with sophisticated SCP by way of right axillary artery (RAxA) perfusion and hypothermic circulatory arrest (HCA)—were reviewed.

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PATIENTS AND METHODS

From April 2001 to September 2011, 1007 consecutive patients underwent open aortic arch repair at the National Cerebral and Cardiovascular Center, Japan. The inclusion criteria included an approach through a median sternotomy, the use of SCP with HCA, and hemi- or partial or total prosthetic replacement of the aortic arch. The patient characteristics are listed in Table 1. The median age was 72 years, and 66.3% of patients were men. The present cohort included 30 patients (3.0%) who had a connective tissue disorder such as the Marfan or Loeys-Dietz syndrome. Of the 1007 patients, 33 (3.3%) had a history of previous cardiac surgery and 38 (3.8%) had undergone previous aortic surgery of the aortic root, ascending aorta, or aortic arch. Aortic pathologic features included acute type A aortic dissection in 230 patients (22.8%). Emergency operations were performed in 259 patients (25.7%), including 76 (7.5%) with shock.

The surgical variables are listed in Table 2. In most patients (73.1%), total arch replacement (TAR) was performed. Concomitantly, coronary artery bypass grafting (CABG) was performed in 186 patients (18.5%) and root replacement in 59 (5.9%).

Data were collected from the medical records for the patients who were followed up in our outpatient department. The data for the others were investigated by telephone or mail. The follow-up rate was 93.0%. The mean follow-up period was 44.9 ± 33.7 months, with a maximum of 128 months. The institutional review board of our center approved the present retrospective study and waived patient consent on the condition that the patients were not identified.

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CKD = chronic kidney disease
COPD = chronic obstructive pulmonary disease
CVD = cerebrovascular disease
HCA = hypothermic circulatory arrest
PND = permanent neurologic dysfunction
RAxA = right axillary artery
SCP = selective cerebral perfusion
TAR = total arch replacement
TEVAR = thoracic endovascular aortic repair

Operative Techniques

The details of our surgical technique of open arch repair have been previously reported.[7-10] Aortic arch aneurysms were approached through a median sternotomy. For establishment of cardiopulmonary bypass, perfusion by way of the distal part of the RAxA in the axilla was routinely used, in conjunction with ascending aortic or femoral artery cannulation. Our routine brain protection was SCP, with perfusion through the RAxA and 2 other arch vessels, with deep or moderate HCA. In the early series, the lowest bladder and nasopharyngeal temperatures during HCA were 16° to 22°C. With the increase in our experience, both temperatures were increased gradually to 28°C, except for high-risk patients with cerebrovascular disease (CVD) or chronic kidney disease (CKD). Thus, for 529 patients (52.5%), moderate HCA of 25° to 28°C was applied. After the introduction of HCA, RAxA perfusion enabled quick conversion to SCP by clamping the innominate artery. After the ascending aorta and aortic arch were opened, balloon-tipped SCP cannulas were inserted into the left carotid and left subclavian arteries.

Open distal anastomosis was performed during HCA of the lower body. In TAR, a stepwise distal anastomosis was frequently used for an easy and secure anastomosis. An invaginated tube graft was inserted into the descending aorta. The proximal end was anastomosed to the descending aorta, and the distal end of the inserted graft was extracted proximally. Debris was flushed from the descending aorta by femoral artery perfusion. The multibranched arch graft was connected to this interposed graft. Then, the systemic circulation was resumed through a side branch of the arch graft. The left subclavian artery was reconstructed using a branch of the main graft, and the patient was rewarmed to 30° to 32°C. The proximal aortic anastomosis was made above the sinotubular junction. Finally, the coronary circulation was initiated by unclamping the main graft. The other 2 arch vessels were reconstructed with branch grafts, and the patient was fully rewarmed.

Definitions

Early mortality was defined as death during the hospitalization or within 30 days postoperatively. Permanent neurologic dysfunction (PND) was defined as the presence of either new focal or global permanent neurologic dysfunction persisting at discharge. Transient neurologic dysfunction was defined as the presence of postoperative reversible motor deficit, confusion, agitation, or transient delirium, with normal computed tomography findings of the brain and resolution of all symptoms before discharge. CVD included a history of cerebrovascular event or a severe carotid artery lesion with more than 75% stenosis or multiple plaques on the ultrasound examination. Chronic obstructive pulmonary disease (COPD) was defined as a forced expiratory volume less than 70% of the normal value or daily use of a bronchodilator. Liver dysfunction was defined as a serum transaminase level more than twice the normal value or a total bilirubin level greater than 2.0 mg/dL. CKD was defined as a serum creatinine level greater than 1.5 mg/dL or a requirement for hemodialysis.

Statistical Analysis

Continuous data are presented as the mean ± standard deviation. Multivariate stepwise logistic analysis was used to identify independent predictors for early mortality and PND. The predictive factors with $P \leq .1$ on univariate analysis were used for subsequent multivariate analysis. The results are presented as the odds ratios and 95% confidence intervals. Cumulative survival and freedom from reoperation rates were calculated using the Kaplan-Meier methods. All statistical analyses were performed using SPSS software (IBM SPSS Inc, Chicago, Ill).

RESULTS

The overall early mortality, including 30-day and in-hospital deaths, was 4.7%. It was 5.0% even for the emergency cases. The cause of early death was low output syndrome in 16 patients (34.0%), sepsis in 15 patients (31.9%), respiratory failure in 10 patients (21.3%), rupture of residual aneurysm in 3 patients (6.4%), and intestinal ischemia in 3 patients (6.4%). On multivariate analysis, the independent risk factors for early mortality were COPD ($P = .041$), liver dysfunction ($P = .014$), CKD ($P < .001$), and concomitant CABG ($P < .001$; Table 3).

Cerebral deficits developed in 102 patients (10.2%) postoperatively, including PND in 35 patients (3.5%) and transient neurologic dysfunction in 67 (6.7%). No spinal cord injury occurred in any patient. The multivariate analysis showed that the independent predictors for PND were CVD ($P = .002$), emergency surgery ($P < .001$), and concomitant CABG ($P = .006$; Table 4).

Prolonged ventilation—for more than 72 hours—was required for 146 patients (14.5%). The length of stay in the intensive care unit and duration of postoperative hospitalization was 3 days (interquartile range, 2-6 days) and 25 days (interquartile range, 19-35 days), respectively.

During the follow-up period, there were 140 late deaths (14.6%). Of these, 13 were aorta-related deaths, including rupture of a descending thoracic aneurysm in 5, an abdominal aortic aneurysm in 5, and sudden death in 3. Of the 10 patients with aneurysm rupture, regular examinations at the hospital had been suspended for 5, and the remaining 5 patients had been observed medically because of their condition or their wish. Cardiac-related deaths occurred in 25 patients (17.9%), including congestive heart failure in 14, acute myocardial infarction in 8, and arrhythmia in 3. Other nonaortic- or noncardiac-related deaths occurred as follows: respiratory failure in 28 patients (20.0%), cancer in 21 (15.0%), cerebrovascular accident in 16 (11.4%), sepsis in 10 (7.1%), gastrointestinal complications in 5 (3.6%), renal failure in 4 (2.9%), accidents in 4 (2.9%), senility in 7 (5.0%), and unknown in 7 (5.0%). The cumulative survival was 80.4% and 71.2% at 5 and 8 years, respectively (Figure 1).

TABLE 1. Patient characteristics (n = 1007)

Characteristic	Value
Age (y)	
Median	72
Range	12-93
Male gender	668 (66.3%)
Hypertension	828 (82.2%)
Diabetes	149 (14.8%)
Hyperlipidemia	381 (37.8%)
Smoking	221 (21.9%)
Cerebrovascular disease	124 (12.3%)
Coronary artery disease	280 (27.8%)
Ejection fraction <30%	14 (1.4%)
COPD	116 (11.5%)
Liver dysfunction	16 (1.6%)
CKD (creatinine ≥ 1.5 mg/dL)	104 (10.3%)
Patients with CKD requiring hemodialysis	16
Connective tissue disorder	30 (3.0%)
Marfan syndrome	25
Loeys-Dietz syndrome	5
Aortitis	23 (2.3%)
Previous cardiac surgery	33 (3.3%)
Aortic redo surgery	38 (3.8%)
Shock	76 (7.5%)
Emergency	259 (25.7%)
Acute dissection	230 (22.8%)

COPD, Chronic obstructive pulmonary disease; *CKD,* chronic kidney disease.

TABLE 2. Surgical procedures

Variable	Value
Extent of graft replacement	
Total arch replacement	736 (73.1%)
Partial arch replacement	28 (2.8%)
Hemiarch replacement	243 (24.1%)
Concomitant procedure	
CABG	186 (18.5%)
Root replacement	59 (5.9%)
Composite graft	47
Aortic valve sparing	12
Aortic valve replacement	85 (8.4%)
Aortic valve repair	2 (0.2%)
Sinotubular junction plication	63 (6.3%)
Mitral valve replacement	5 (0.5%)
Mitral valve repair	10 (1.0%)
Tricuspid annuloplasty	9 (0.9%)
Maze	6 (0.6%)
Intraoperative variables	
Lower body circulatory arrest time (min)	55.5 ± 17.6
Selective cerebral perfusion time (min)	129.4 ± 67.0
Myocardial ischemic time (min)	139.3 ± 53.9
Cardiopulmonary bypass time (min)	240.3 ± 99.2
Core temperature at HCA	
Moderate (25°-28°C)	529 (52.5%)
Deep (<25°C)	478 (47.5%)

CABG, Coronary artery bypass grafting; *HCA,* hypothermic circulatory arrest.

Late aortic operations related to the previously repaired arch segment were required for false aneurysm of the anastomotic site in 12 patients and for graft infection in 2. Of the patients with false aneurysms at the distal anastomotic site, 8 underwent TEVAR. Four patients who developed false aneurysms at the proximal anastomotic site and two who developed graft infection underwent redo graft replacement of the aortic arch. Freedom from reoperation for the initially repaired arch segment was 98.0% and 96.9% at 5 and 8 years, respectively (Figure 2, *A*). Other late aortic reoperations unrelated to the initial aortic arch replacement included composite graft replacement in 6, valve-sparing root replacement in 2, completion arch replacement after hemiarch repair in 5, descending aortic replacement in 36, thoracoabdominal aortic replacement in 28, abdominal aortic repair in 59, and endovascular repair of the descending aorta in 46 and the abdominal aorta in 10 patients. Freedom from all late aortic reoperations at 5 and 8 years was 78.0% and 71.7%, respectively (Figure 2, *B*).

DISCUSSION

Open aortic arch repair remains challenging, with some difficulties. In most patients, the etiology of the arch aneurysm is atherosclerosis; therefore, most of patients are quite elderly and have many atherosclerotic lesions. However, recent advances in brain protection, surgical techniques, anesthesia, and critical care have improved the surgical outcomes. Thus, antegrade SCP with HCA has achieved widespread acceptance as a reliable brain protection technique.[1-4] Recent reports have suggested some refinement of surgical techniques, in addition to SCP, and have demonstrated lower mortality rates of 4% to 8%.[4,11-15] A gradual increase of the core temperature during HCA from deep to moderate hypothermia has been encouraged to avoid deep hypothermia-associated coagulopathy and reduce the inflammatory substances associated with prolonged cardiopulmonary bypass.[4,16] Our current basic management of the core temperature during HCA with SCP is moderate hypothermia, which has produced favorable outcomes in aortic arch surgery.[17] However,

TABLE 3. Risk factors for in-hospital mortality

Factor	Univariate *P* value	Multivariate *P* value	Multivariate OR	Multivariate 95% CI
Previous cardiac surgery	.063	.234		
CAD	<.001	.223		
COPD	.009	.041	2.157	1.030-4.518
Liver dysfunction	.007	.014	5.629	1.419-22.331
CKD (creatinine > 1.5 mg/dL)	<.001	<.001	4.637	2.392-8.988
Concomitant CABG	<.001	<.001	3.424	1.837-6.382
Deep hypothermia (<25°C)	.089	.476		

OR, Odds ratio; *CI,* confidence interval; *CAD,* coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *CKD,* chronic kidney disease; *CABG,* coronary artery bypass grafting.

TABLE 4. Risk factors for permanent neurologic dysfunction

Factor	Univariate *P* value	Multivariate *P* value	OR	95% CI
Elderly (age ≥ 75 y)	.073	.068		
CVD	<.001	.002	3.374	1.589-7.162
CKD (creatinine > 1.5 mg/dL)	.081	.201		
Emergent surgery	.002	<.001	4.013	1.887-8.535
Concomitant CABG	.044	.006	3.119	1.379-7.057

OR, Odds ratio; *CI,* confidence interval; *CVD,* cerebrovascular disease; *CKD,* chronic kidney disease; *CABG,* coronary artery bypass grafting.

deep hypothermia of about 22°C, which has a great advantage for more secure brain, spinal cord, and visceral organ protection during HCA, is still used in selected higher risk patients with severe CVD and CKD or requiring a longer duration of HCA of the lower body because of anticipated difficulty in performing the distal anastomosis to the descending aorta.[10]

To the best of our knowledge, the present study is the largest scale study of open aortic arch replacement. The period of surgery was limited to 10 years, and a similar surgical technique—including SCP with RAxA perfusion—was used for all cases. Thus, we believe the outcome is worthy of assessment. The mortality rate of 4.7% is comparable to those of recent other reports,[4,11-15] with a range of 4% to 9%, although more than 70% of our patients underwent more extensive TAR and 25% were emergency cases. In addition, 15.5% of the patients were older than 80 years, and 24.4% required concomitant coronary or aortic root surgery. At least 10 surgeons—including some residents—were involved in the present series of arch repairs. In terms of the incidence of neurologic deficits, although the overall rate of 10.2% was similar, the stroke (PND) rate of 3.3% was lower than those of other reports (4%-7%). We believe our

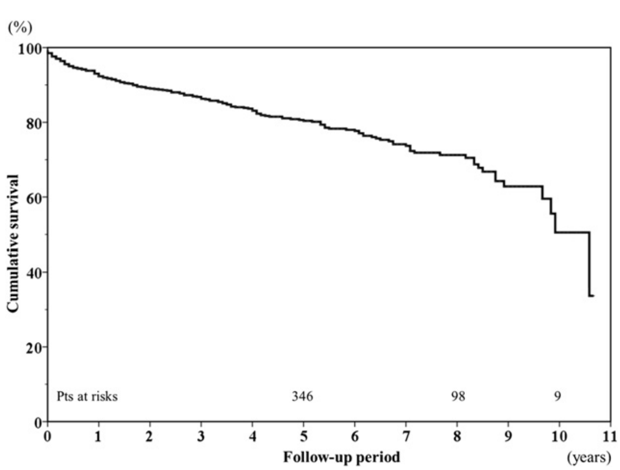

FIGURE 1. Survival curve for all patients by Kaplan-Meier method. Cumulative survival rate was 80.4% and 71.2% at 5 and 8 years, respectively.

outcomes have been so satisfactory that our contemporary aortic arch replacement technique should be recognized as the standard repair for arch aneurysms.

With regard to risk factor analyses, the independent risk factors for early mortality were COPD, liver dysfunction, CKD, and concomitant CABG. The number of in-hospital deaths from respiratory failure, in particular, interstitial pneumonia or pulmonary fibrosis, has recently increased with the increase in patient age. These serious complications seem to be untreatable after their occurrence postoperatively. For these patients, arch TEVAR should be recommended. Regarding CKD and concomitant CABG, most such patients have more severe atherosclerosis and are critically compromised hosts, with diabetes and hemodialysis. For some of these patients, percutaneous coronary intervention before arch repair might be a good option to improve the outcome.

In terms of PND, CVD, emergency operation, and concomitant CABG were risk factors. The former 2 factors are easily recognized as risk factors for stroke. More meticulous brain protection with deep hypothermia is recommended for such conditions. A requirement for concomitant CABG is another risk factor for stroke. We believe this did not result from technical problems, but rather that these patients tended to have severe atherosclerotic vascular lesions, particularly in the aorta, arch vessels, or intracranial arteries, which might be related to the occurrence of stroke.

Regarding the technical aspect, our aortic arch repair technique has some characteristic features. The first is our routine use of RAxA perfusion by simple direct cannulation in the axilla.[7] It can be established easily and quickly, even in an emergency setting, and can prevent the cerebral emboli caused by retrograde femoral artery perfusion. Right-sided SCP through the RAxA can also be quickly achieved by simple clamping of the innominate artery. The second characteristic strategy is a preference for the use of stepwise distal anastomosis with a mini- or standard elephant trunk insertion for easier and more secure anastomoses for TAR.[8] The third technique is separate reconstruction of the arch vessels using a multibranched prosthetic graft for TAR.[2] We are encouraged to thoroughly remove the atheromatous arterial wall around the origin of the arch vessels and to perform the anastomosis at less atherosclerotic parts of the arch vessels, resulting in fewer embolic cerebrovascular events.

Long-term survival after open aortic arch repair has been demonstrated in some other reports. Kazui and colleagues[2] reported an actuarial survival at 5 and 7 years of 79% and 77%, respectively, and a recent report by Patel and colleagues[12] demonstrated a 12-year survival of 51.2%. Their survival curves were similar to ours, with 80.4% and 71.7% survival at 5 and 8 years, respectively. The median patient age in the present series was 72 years, and some of our

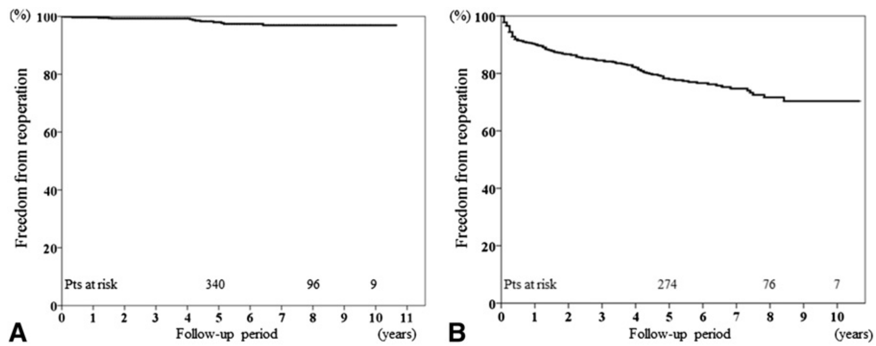

FIGURE 2. A, Kaplan-Meier analysis of freedom from reoperation related to initial arch repair. The rate of freedom from reoperation for the initially repaired arch segment was 98.0% and 96.9% at 5 and 8 years, respectively. B, Kaplan-Meier analysis of freedom from all aortic reoperation, including other segments. Freedom from late aortic surgery was 78.0% and 71.7% at 5 and 8 years, respectively.

patients died of cancer. Thus, we believe the long-term survival rate was acceptable in our patient cohort.

Furthermore, reoperation related to the initial arch repair during follow-up—for anastomotic false aneurysm or graft infection—was very rare. Most secondary aortic interventions after open arch repair were necessary for the other aortic lesions, including the aortic root, descending aorta, or abdominal aorta. For anastomotic false aneurysm, open repair or TEVAR can be successfully performed. In particular, TEVAR is easily applied to such limited lesions, with the proximal landing zone in the arch graft.

However, endovascular treatments have expanded in the past decade, and in 2008 some commercially available devices for TEVAR were introduced in Japan. Since then, our surgical strategy for aortic arch aneurysm has gradually shifted toward TEVAR. Currently, open aortic repair remains our basic surgical option, because it has been well established and has provided satisfactory early and long-term outcome. However, for its **lesser invasiveness**, this new surgical technique—including hybrid TEVAR—has been applied predominantly in limited high-risk patients, including the elderly (>75 years old), patients with severe comorbidities (eg, impaired cardiac, pulmonary, liver, or renal function), and those with a history of previous cardiac surgery.[18] Some reports of hybrid arch procedures have demonstrated an overall mortality rate of 3.2% to 11% and a stroke rate of 0% to 11%.[5,6,19,20] A recent meta-analysis of 463 patients who underwent hybrid arch surgery reported a 30-day mortality of 8.3% and an incidence of stroke and paraplegia of 4.4% and 3.9%, respectively.[21] Although the study included high-risk patients unsuitable for conventional open aortic repair, the mortality was slightly greater rather than the current results of open arch surgery, including in our study. In addition, the meta-analysis had a mean follow-up period of 18.9 to 61 months, leaving the long-term results still unclear.

Several innovations in endovascular devices and techniques have occurred within the past few years. For instance, the chimney graft technique, involving the supra-aortic branches, which can treat up to zone 0 lesions without sternotomy, was recently introduced. Gehringhoff and colleagues[22] reported their experience using this technique for aortic arch pathologic features in 9 patients. In that report, 1 patient (11.1%) underwent surgical arch replacement because of a persistent type I endoleak, and 1 early death (11.1%) occurred. However, the safety and durability of these new techniques remains unclear, and future studies are necessary.

Comparing the outcomes between open aortic repair and TEVAR is complicated by the patient selection bias. In general, arch TEVAR has been indicated for higher risk patients with severe comorbidities. Milewski and colleagues[19] reported that hybrid arch procedures have their primary benefit in high-risk cases, especially elderly patients previously considered at prohibitively high risk to undergo conventional open arch repair. In the present analysis, the risk factors for early mortality were COPD, liver dysfunction, and CKD. We agree that arch TEVAR is a beneficial therapeutic option for patients expected to experience high mortality and morbidity with conventional open arch repair. However, we are skeptical about the adoption of this new technology for patients with a reasonable operative risk and younger patients, especially those with connective tissue disorders, because the mid- and long-term outcomes of TEVAR are still unclear. We have experienced extremely difficult and high-risk surgical conversion after TEVAR required for endoleak, infection, and esophageal fistula in some patients. These less-invasive TEVAR repairs, including hybrid procedures, should still be applied predominantly in high-risk patients with advanced age or many comorbidities.

The present study had some limitations. It was a retrospective study of a single group of patients who underwent open aortic arch repair with SCP. To compare the results of the 2 surgical strategies more clearly, a multicenter, prospective, randomized study is required.

CONCLUSIONS

A well-established contemporary open aortic arch repair using SCP with hypothermia produced satisfactory early and long-term outcomes and remains a standard therapy with good long-term durability. It is highly recommended, except for high-risk patients.

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